Amendments to the Specification

Please replace the paragraph under **Cross-Reference to Related Applications** on page 1 with the following amended paragraph:

This application ~~claims the benefit of~~ is a U.S. National Phase Application of International Application PCT/US2004/021646, filed July 7, 2004, which claims benefit of US Provisional Application 60/484,655, filed July 7, 2003, both of which are ~~is~~ hereby incorporated by reference in their ~~its~~ entirety.

Please replace the paragraph on page 8, lines 14-16, with the following amended paragraph:

~~**Figures 7A-B**~~ **Figure 7.** $CD4^+CD40^+$ T cell increases are predictive of rheumatoid arthritis. ~~7A. Rheumatoid~~ The left panel is a rheumatoid arthritis patient. ~~7B. Control~~ The right panel is a control patient. See Example 4 for details.

Please replace the paragraph on page 8, lines 17-18, with the following amended paragraph:

~~**Figures 8A-B.**~~ **Figure 8.** $CD4^+CD40^+$ T cell increases are predictive of asthma. ~~8A. Control~~ The left panel is a control patient. ~~8B. Asthma~~ The right panel is an asthma patient. See Example 5 for details.

Please replace the paragraph on page 25, lines 20-30, with the following amended paragraph:

Staining. T cells were purified from excised spleens of NOD, NOR or BALB/c mice at the ages indicated, incubated on nylon wool wetted columns with HBSS-5%BSA for 45 min. Purified T cells (> 92% $CD3^+$) were washed with HBSS-5% BSA, treated with 2.4.G2, anti-Fc-receptor blocking antibody, then stained with directly conjugated FITC-anti-CD40, $1C10^{37}$, PE-anti-TCR$\alpha\beta$, H57.597 or PE-anti-CD3, 145.2C11 (Pharmingen, San Diego, CA), and Cy-Chrome™-anti-CD4 ~~CyChrome™-anti-CD4~~, H129.19 (Pharmingen). Cells were run on a

~~Becton-Dickinson FACScalibur~~ Beckton-Dickinson FACScalibur™ and assayed using CellQuest™ software. In some cases, splenic T cells were incubated with biotin-anti-CD3 (145.2C11), washed with HBSS, incubated with Miltenyi (Auburn, CA) magnetic avidin beads and passed through a Miltenyi selection column as per manufacturer's instructions. Purified T cells were then stained as described.

Please replace the paragraph on page 26, lines 3-14, with the following amended paragraph:

Adoptive Transfers. T cells were nylon wool-purified from spleens of diabetic and pre-diabetic NOD females, incubated with biotinylated anti-CD40 (1C10 produced in-house), biotinylated anti-Vα3.2, or biotinylated anti-Vα8.3 (both from Pharmingen). The cells were washed with PBS then incubated with magnetic avidin beads (Miltenyi, Auburn, CA) and passed over magnetic purification columns (Miltenyi). Purified T cells were eluted and determined to be >98% pure by flow cytometry. CD8+ T cells were removed by incubating T cells with a magnetic conjugated anti-CD8 antibody (Miltenyi) then passed over a magnetic column (Miltenyi). Purified $CD4^+CD40^+$ T cells, ~~$1.5x10^6$,were~~ $1.5x10^6$, were injected intraperitoneally, i.p., into 9-day old NOD.scid recipients. Control animals received $CD4^+CD40^-$ T cells, $1.5x10^6$ cells. Animals were monitored for diabetes onset by blood glucose *(b.g.)* determinations. Diabetes was considered to be a *b.g.* level of >150 mg/dl.

Please replace the paragraph under **Example 4** on page 34, lines 5-15, with the following amended paragraph:

$CD4^+CD40^+$ T cell increases are predictive of rheumatoid arthritis. Peripheral blood, 10 ml, was drawn by phlebotomy from clinically identified rheumatoid arthritis (RA) patients. Blood was mixed with phosphate buffered saline (PBS) 1:1 then layered on ~~Ficoll~~ FICOLL™ and centrifuged to isolate lymphocytes. Lymphocytes were collected, washed with PBS and directly stained with Cy-chrome conjugated anti-CD4 and FITC-conjugated anti-CD40. Stained T cells were analyzed using a ~~FACScalibur~~ FACScalibur™ Flow Cytometer. Levels of T cells were compared from RA patients and control patients. As in type 1 diabetes, $CD4^+CD40^+$ T cell

levels are greatly exaggerated, 56% versus 12%, in RA compared to controls. Thus $CD4^+CD40^+$ T cell increases are predictive of rheumatoid arthritis. Results are shown in ~~Figures 7A and 7B~~ Figure 7.

Please replace the paragraph under **Example 5** on page 34, lines 17-26, with the following amended paragraph:

$CD4^+CD40^+$ T cell increases are predictive of asthma. Peripheral blood, 10 ml, was drawn by phlebotomy from clinically identified Asthma patients. Blood was mixed with phosphate buffered saline (PBS) 1:1 then layered on ~~Ficoll~~ FICOLL™ and centrifuged to isolate lymphocytes. Lymphocytes were collected, washed with PBS and directly stained with Cy-chrome conjugated anti-CD4 and FITC-conjugated anti-CD40. Stained T cells were analyzed using a ~~FACScalibur~~ FACScalibur™ Flow Cytometer. Levels of T cells were compared from Asthma patients and control patients. As in type 1 diabetes, $CD4^+CD40^+$ T cell levels are greatly exaggerated, 38% versus 8%, in RA compared to controls. Thus $CD4^+CD40^+$ T cell increases are predictive of asthma. Results are shown in ~~Figures 8A and 8B~~ Figure 8.

Please replace the paragraph under **Example 6** on pages 34, line 28, to page 35, line 4, with the following amended paragraph:

$CD40^+CD4^+$ T cells are predictive for Human type 1 diabetes. Blood was drawn from 25 clinically diagnosed type 1 diabetic patients and from 20 non-diabetic controls. Whole blood was diluted with PBS, suspended on Hypaque-~~Ficoll~~ FICOLL™, centrifuged for 10 min at 5000RPM. Leukocytes were isolated and stained with directly conjugated anti-CD3, anti-CD4 and anti-CD40. Cells were assayed through a ~~FACScalibur~~ FACScalibur™ flow cytometer. Cells were gated on CD3 (T cell marker) and analyzed for CD4 and CD40 levels. Controls **(A)** and Diabetics **(B)** are represented. Total percent of $CD4^+CD40^+$ /$CD4^+CD40^+$ + $CD4^+CD40^-$ are represented **(C)**. This measurement is predictive of diabetes. Results are presented in Figures 9A-C.

Please insert the attached abstract after page 40.